Introduction to OCBQ, DMPQ, and Lot Release

CBER 101

Jay Eltermann

Division of Manufacturing and Product Quality

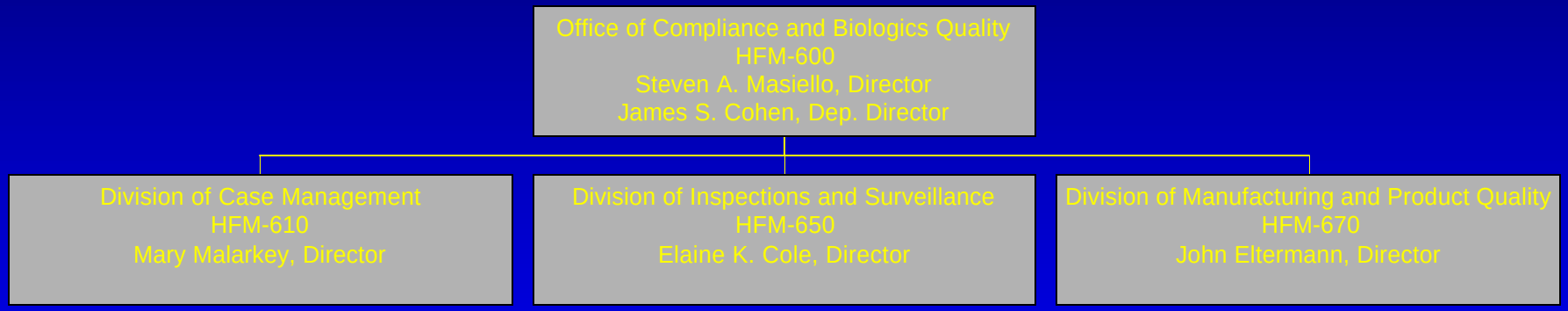
Overview of this presentation

- OCBQ overview
- DMPQ responsibilities
  - Reviews
  - Inspections
  - Meetings
  - Lot release
  - Training
  - Guidance documents
- Future activities and new directions

Office of Compliance and Biologics Quality

- 3 divisions, 104 employees
- Diverse range of cross-cutting functions which require close collaboration with the product offices
- Responsible for issues throughout the product life cycle, from IND to post marketing surveillance
- CBER interface with ORA and districts

OCBQ Organization Chart



Division of Case Management

- Reviews and evaluates compliance action recommendations including suspension, revocation, Warning letters
- Conducts review of export applications
- Blood, plasma, and tissue enforcement actions
- Reviews promotional labeling and advertising

Division of Inspections and Surveillance

- Manages Bioresearch monitoring and complaints for IND products
- Manages emergency and product shortage program
- Reviews Biological Product Deviation Reports
- Coordinates CBER activities with ORA, including Team Biologics
- Develops and updates compliance programs

Division of Manufacturing and Product Quality

- Review of manufacture's submissions such as applications, supplements, INDs, DMFs
- Generally: facility/equipment/cGMPs
- Conduct and lead pre-approval inspections
- Administer CBER's lot release program
- Provides training on GMP and inspection issues
- Active role in policy and guidance development

DMPQ Review Responsibilities - Products by review branch

- MRB1 (C. Kelley)
- Bacterial Vaccines
- Cytokines
- Monoclonal Antibodies
- Allergenic Extracts
- In-vitro diagnostic kits

- MRB2 (J. Finkbohner)
- Viral Vaccines
- Plasma fractionation
- Hematologic Therapeutics
- Blood Grouping reagent
- Gene Therapy

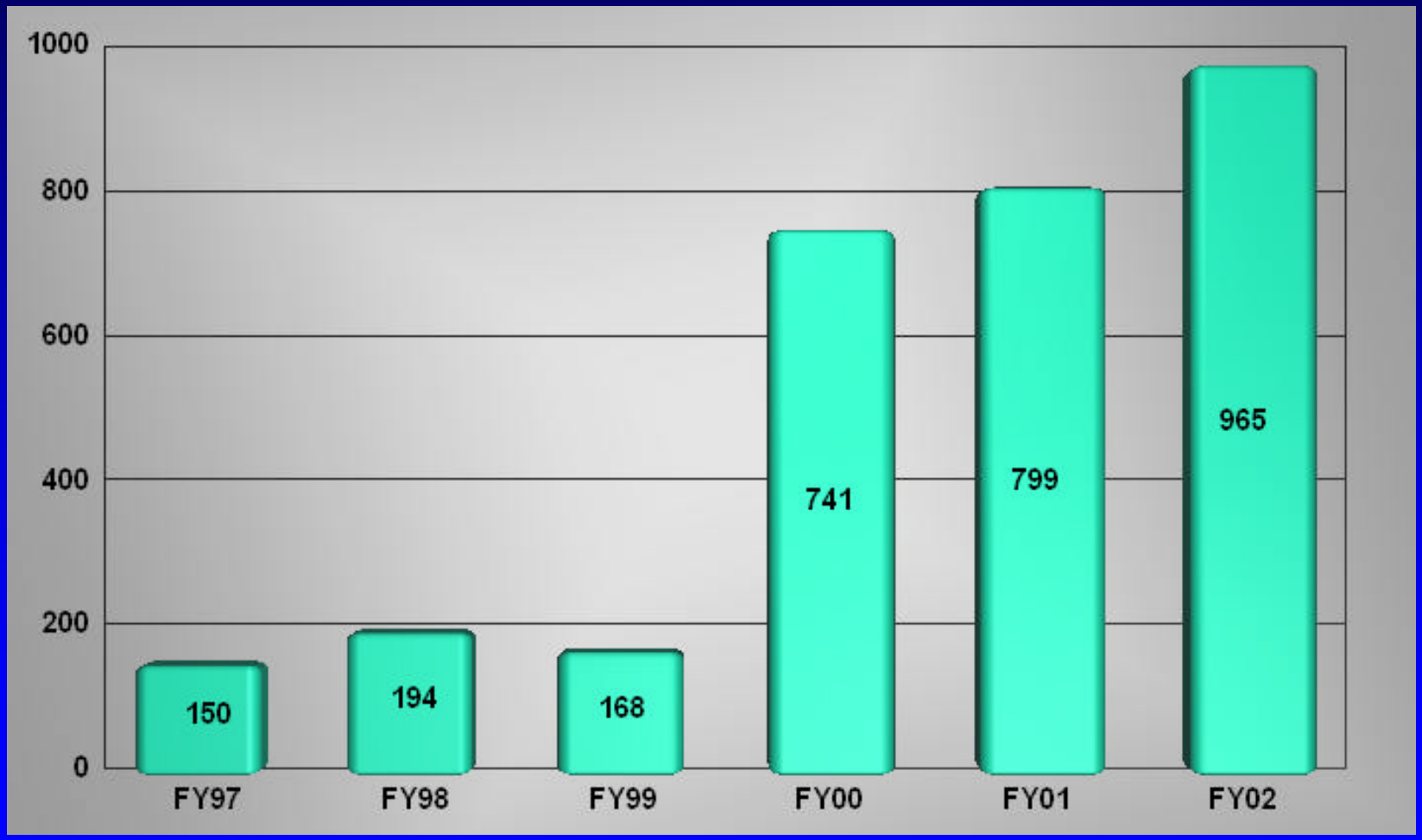
DMPQ Responsibilities in the Review Process

- DMPQ reviewers may be part of a larger CBER review committee or DMPQ may have sole responsibility for review/approval
- DMPQ is responsible for reviewing issues in CMC as well as responsibility for the review of the Establishment Description Section

DMPQ Responsibilities in the Review Process

- Focal point for process control, equipment process capability, process validation issues, and GMP assessments
- Handles administrative reviews such as licensing issues (corporate name changes, mergers, etc.)
- DMPQ leads pre-approval inspections

Submissions Received by DMPQ



DMPQ Responsibilities in the Review Process

- INDs/DMFs - consult reviewers; administratively handles Type V DMFs
- Meetings - pre-facility meetings at any stage in the process (IND or BLA) for new or renovated facilities
- Conduct meetings according to CBER SOPP 8110.1

DMPQ - Role in Policy and Guidance Documents

- Policy and procedures: members of CBER's coordinating committees
- Work on guidance documents such as:
  - ICH Q7A
  - CMC guidance (and now CTD)
- Technical issues such as:
  - Barrier Isolators
  - Aseptic Processing
  - Environmental Monitoring

DMPQ Role in Training

- Participated in training of Team Biologics during transition of biennial inspection responsibility
- Through the Center's training program, DMPQ provides training on inspections, cGMPs/ and other technical issues
- Presentations at numerous industry meetings and workshops

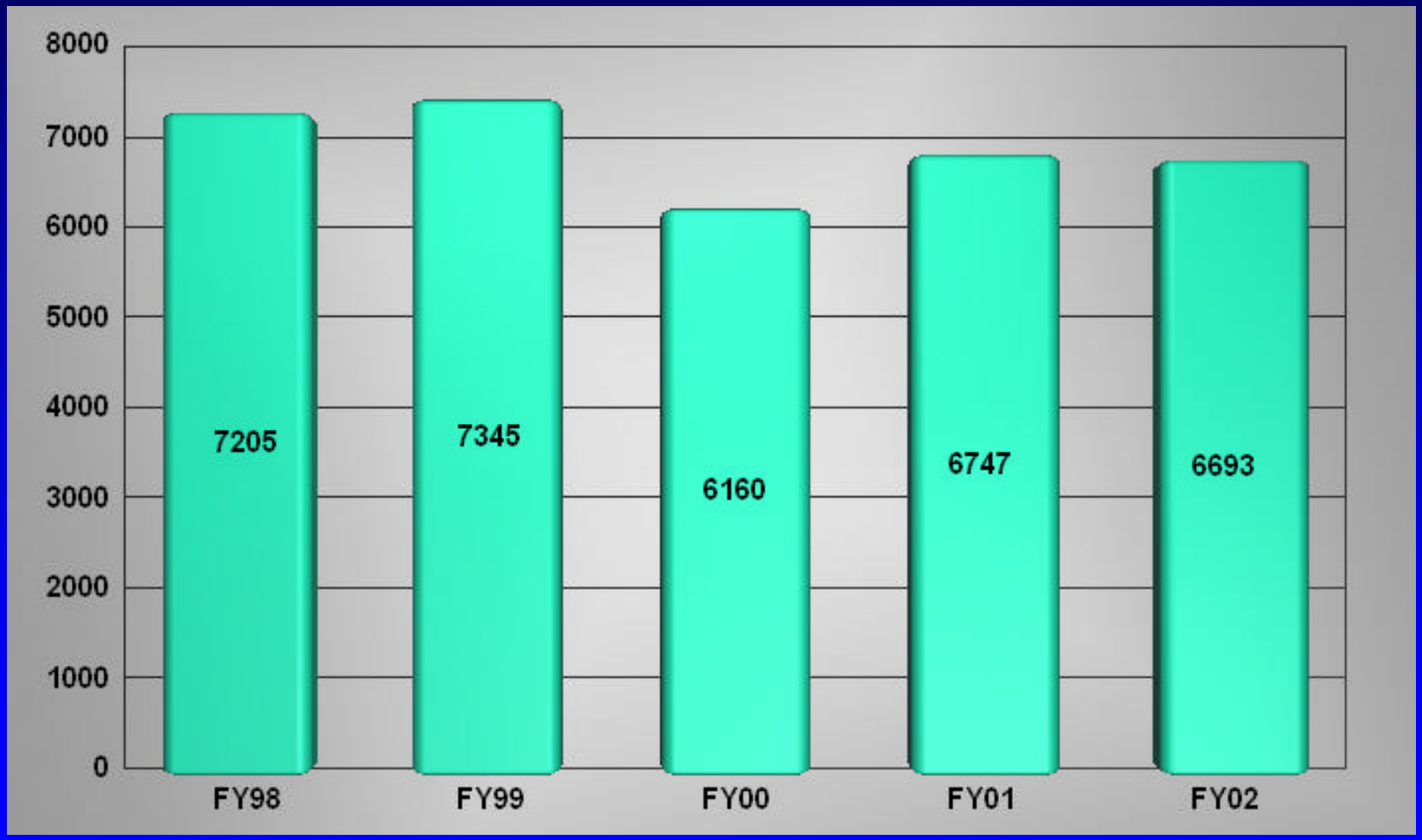
Introduction to Lot Release

- 21 CFR Part 610, Subpart A
- Sets requirements for each applicable test to be performed by the manufacturer
- States that samples and protocols need to be submitted to CBER
- States that no lots* may be distributed unless released by CBER
- Specific tests found in other sections

Lot Release - Overview

- Manufacturing and testing information for each lot of product needs to be reviewed by CBER prior to distribution
- Manufacturers submit lot release protocols and samples
- Some products are exempt from lot release

Final Actions Completed (Releases and Withdrawals)



Lot Release - Overview

- Protocol may be for bulk, concentrates or final container material
- Some products have releases at several stages (release at conc. and final container)
- Some products are released at the bulk stage and used for multiple filling (no final container material is submitted)
- IVDs are released as complete kits*

Lot Release Process

- Samples and protocols submitted to CBER, together or separate
- Information entered into CBER database
- Protocols reviewed by scientific staff to ensure specifications met
- Product samples are available for confirmatory testing
- Protocol package is reviewed by Product Release Branch and the lot is released

Exemptions from lot release

- Manufacturer submits supplement requesting exemption. Criteria announced in July 20, 1993 FR Notice
  - History of lots manufactured
  - Fate of these lots
  - Complaints, corrective actions
  - Description of major process changes
- May 1996 FR Notice: Biotech products exempt

Product lots Submitted in Support of a Supplement

- Some manufacturing changes require lots to be submitted to assess impact on product quality
- Protocols should include the Reference Number
- For PAS, lots not released until approval
- For CBEs or CBE-30s, may be released prior to supplement approval

DMPQ - Future Activities

- Meet the challenges for licensing products for counter-terrorism and novel therapies
- Earlier involvement in the review process IND stage)
- Streamlining our reviews, administrative actions, and lot release to meet PDUFA and MDUFMA
- Implementation of the GMP initiatives
- Guidance document development

Summary

- Many roles of DMPQ within CBER
- Cross-cutting nature of our responsibilities and integral part of the review process
- Involved as part of the review team on many CBER submissions
- Lot Release and certain manufacturing supplements – DMPQ lead
- Lead for the preapproval inspections

Contact Information

- Reviews/meetings:
  HFM-670
  (301) 827-3031 (301) 827-3536 fax
- Lot release issues
  HFM-672
  Product Release Branch -D. Parshall
  (301) 594-6513